

1/22

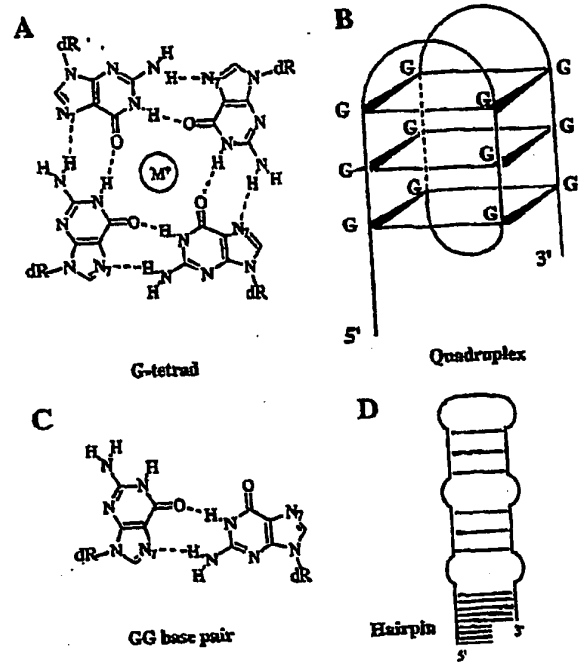


Fig. 1

2/22

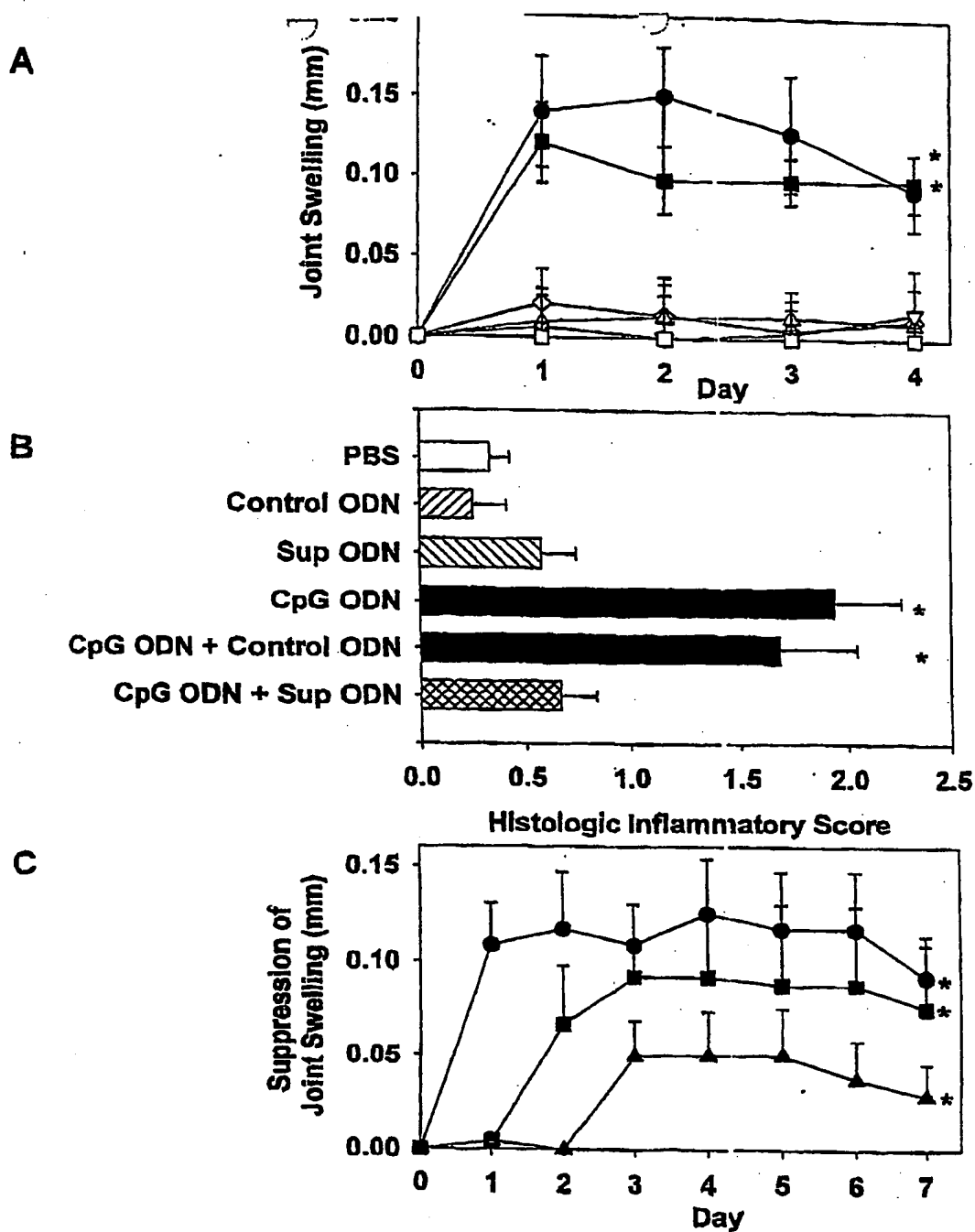


Fig. 2

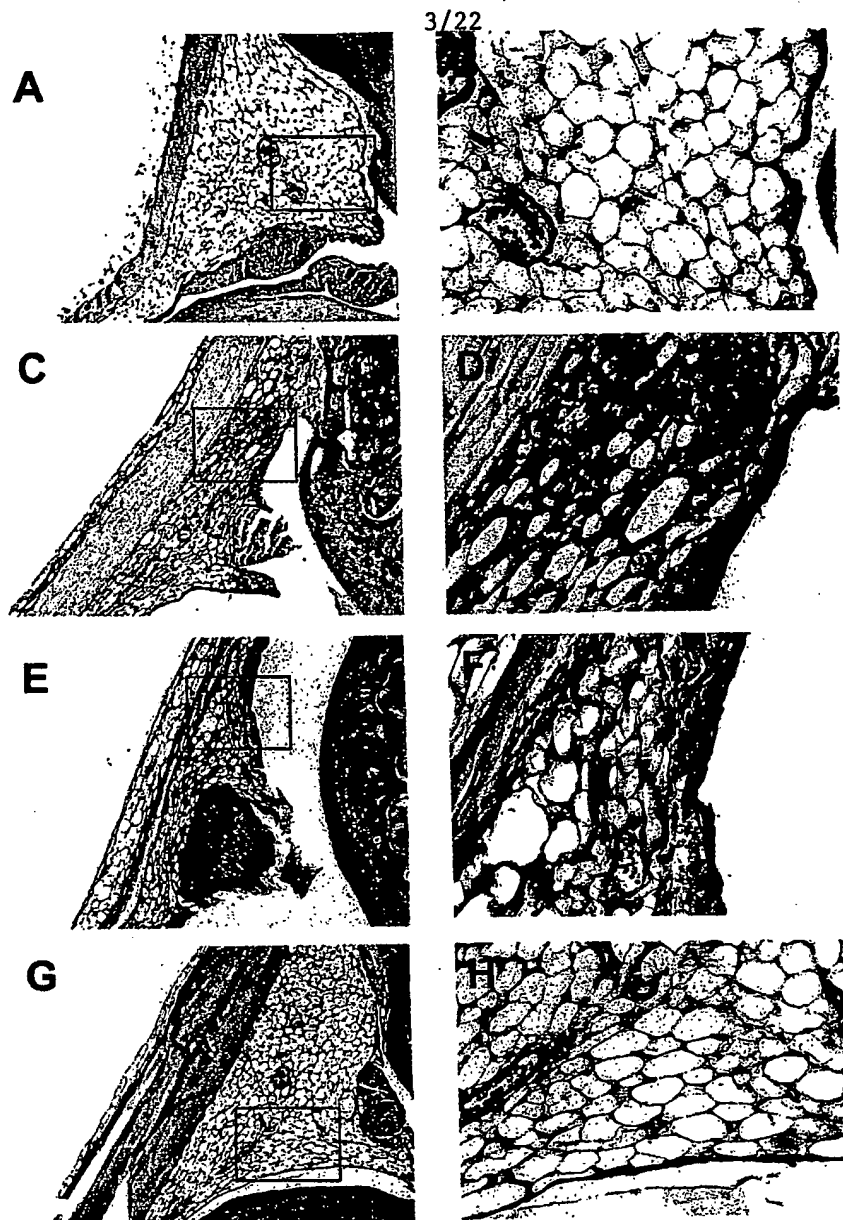


Fig. 3

4/22

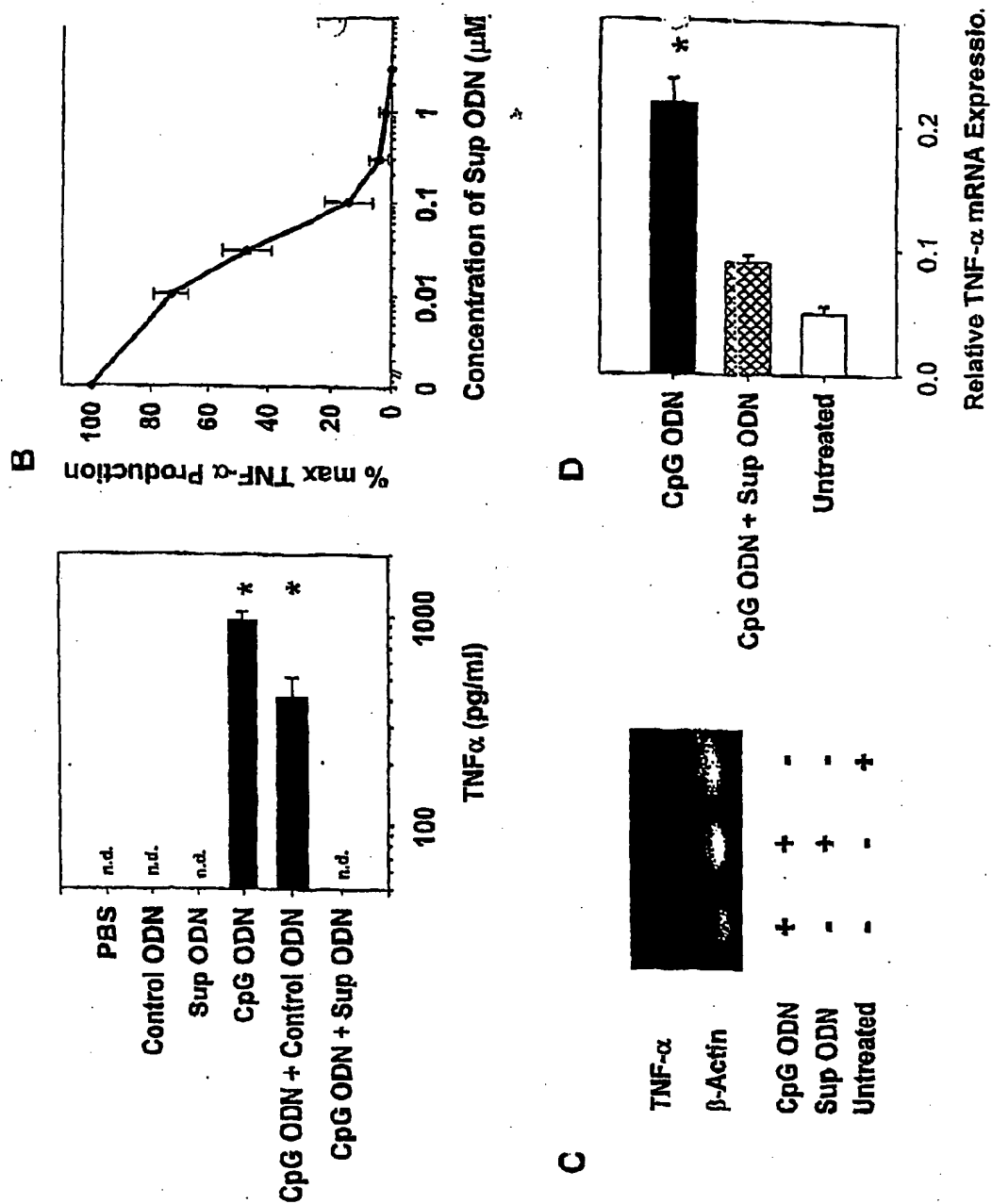


Fig. 4

5/22

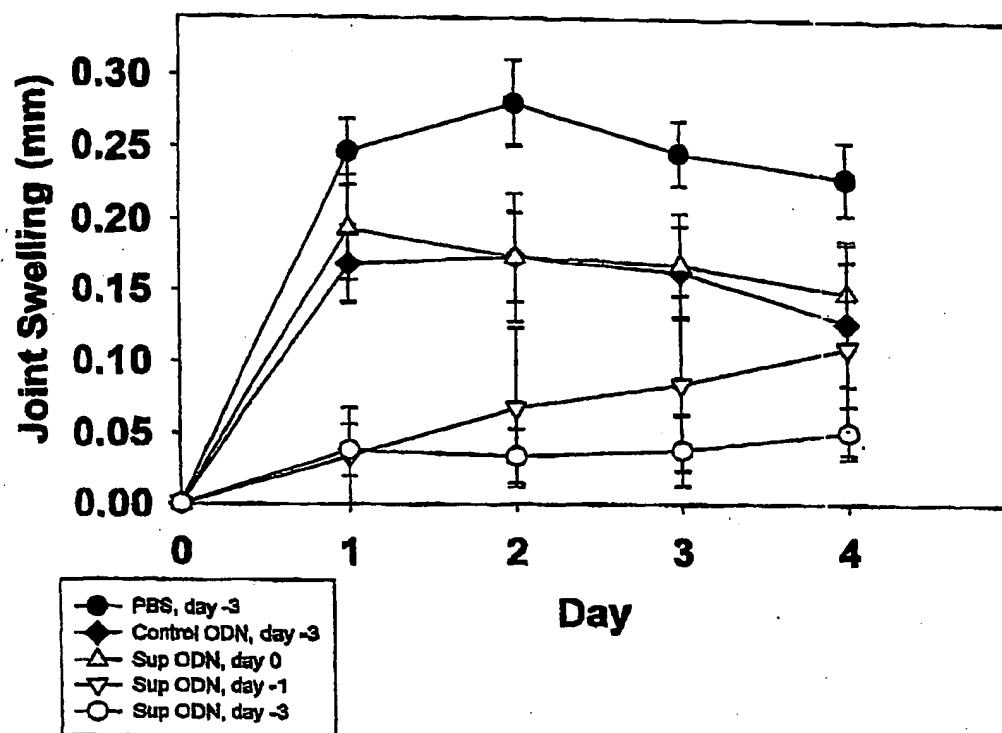
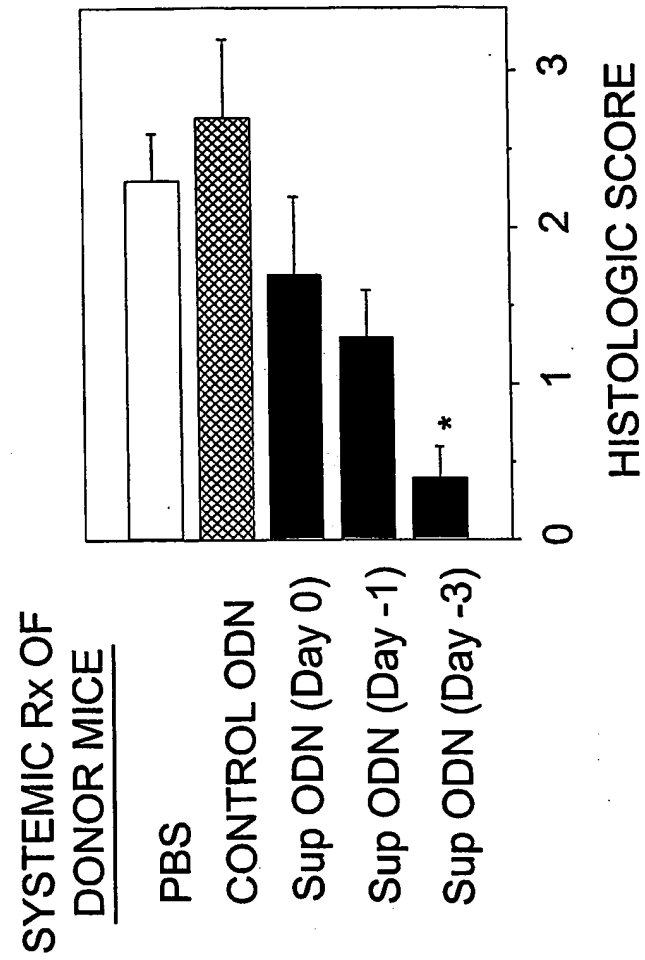


Fig. 5

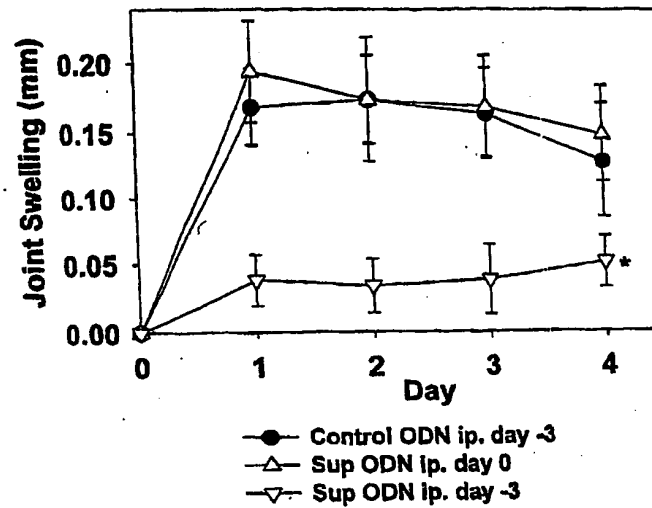
6/22

Fig 6

7/22

systemic effect of Sup ODN on CpG-Induced Arthritis

A



B

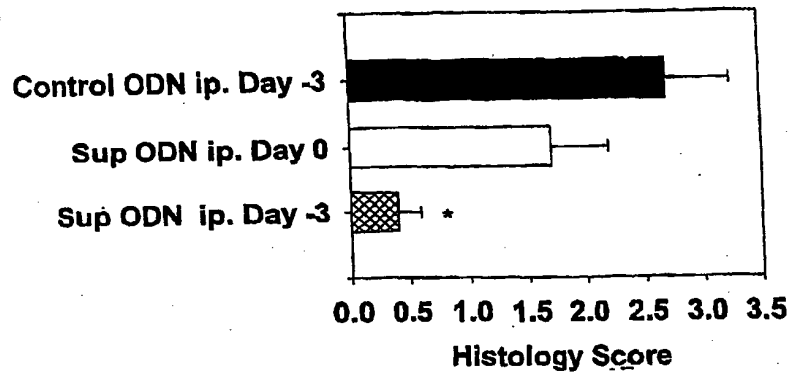


Fig. 7

8/22

Fig. 8A

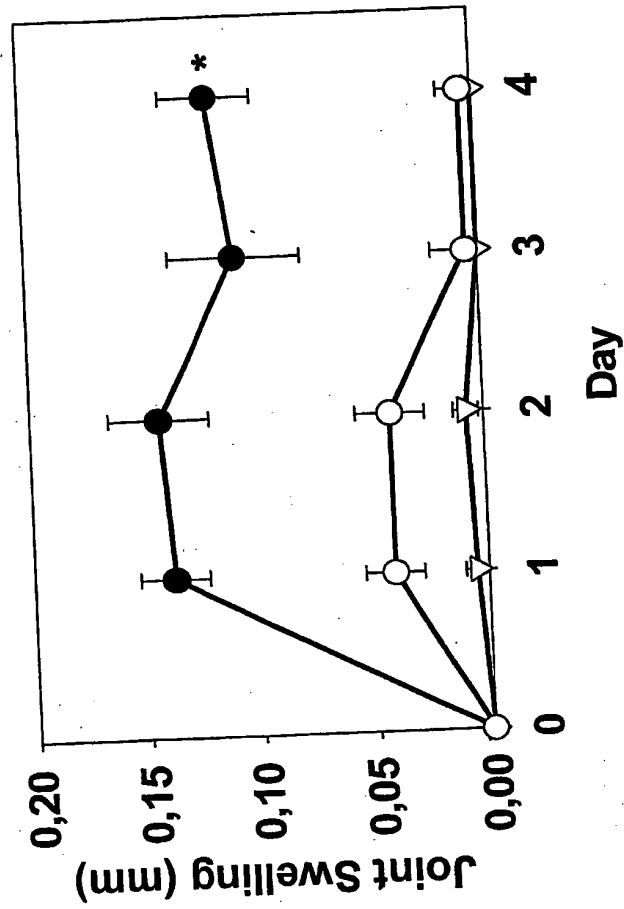
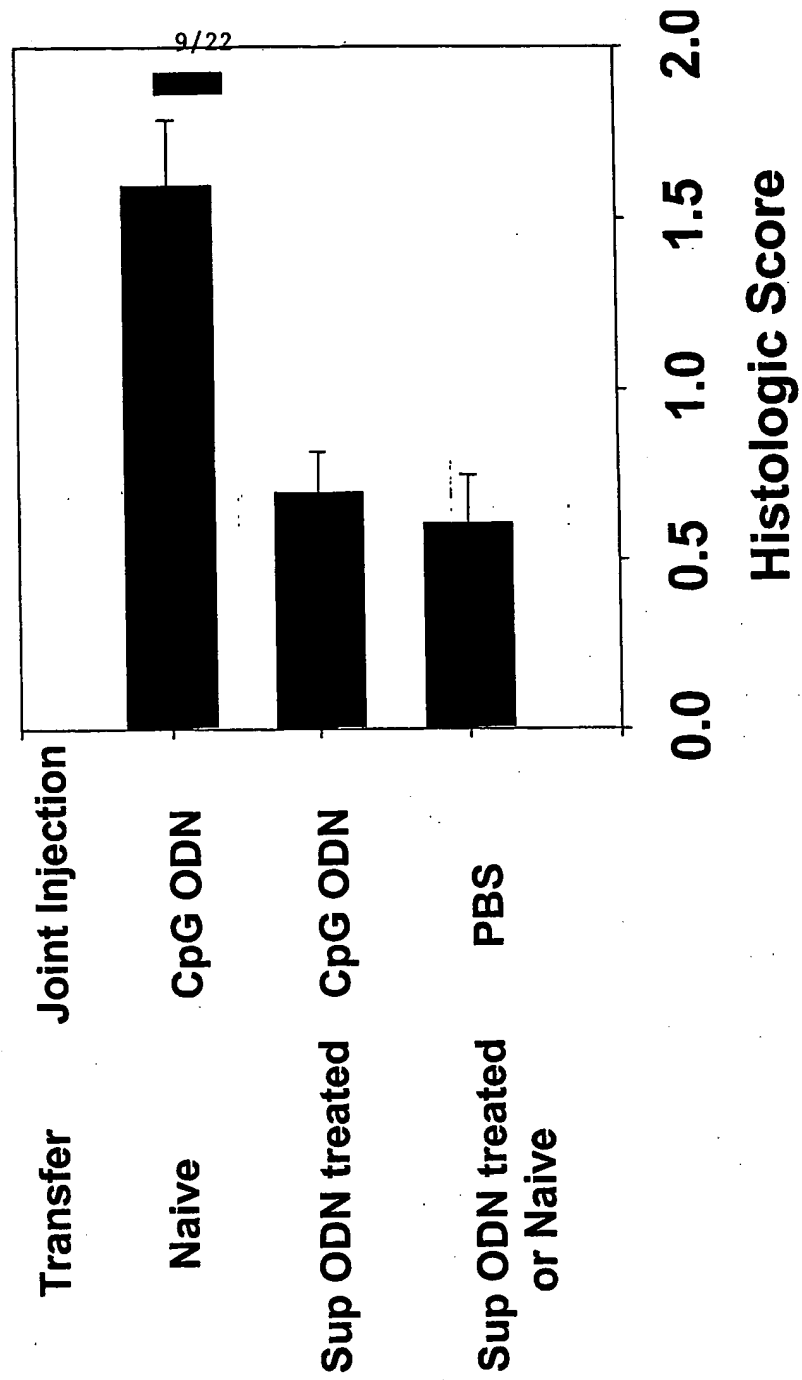


Fig 8B
Spleen cell Transfer



10/22

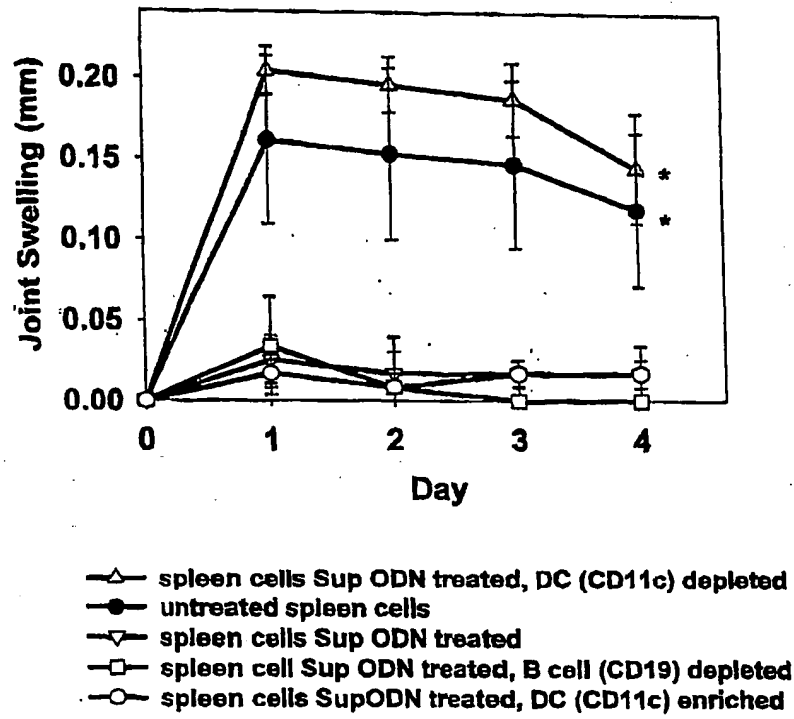
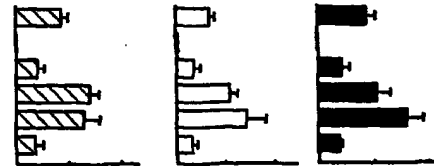


Fig. 9

11/22

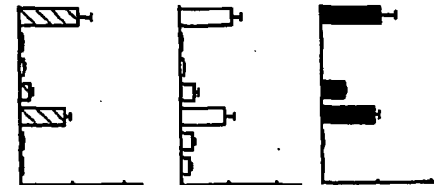
a Mammalian DNA suppresses CpG DNA induced immune activation

Bacterial DNA
Mammalian DNA
Bacterial DNA + Mammalian DNA
CpG ODN
CpG ODN + Bacterial DNA
CpG ODN + Mammalian DNA

**b Telomeric TTAGGG repetitive motif is suppressive**

Ellipticity (mdeg/abs)

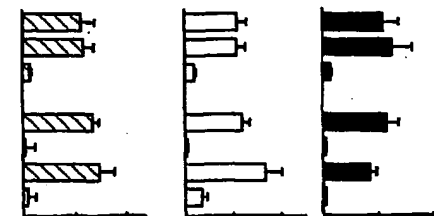
CpG ODN 1.4
CpG ODN + (TTAGGG)₄ 7.1
CpG ODN + (TTAGGG)₃ 4.8
CpG ODN + (TTAGGG)₂ 2.6
CpG ODN + (TTAGGG)₁ 1.2
CpG ODN + TCAACCTTCATTAGGG 3.4
CpG ODN + TTAGGGTCAACCTTCA 3.4

**c Suppressive motif is active in trans and cis***Trans*

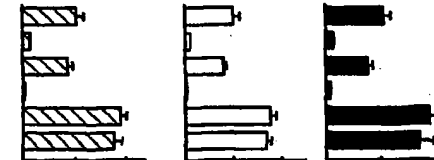
CpG ODN
CpG ODN + Control ODN
CpG ODN + Suppressive ODN

Cis

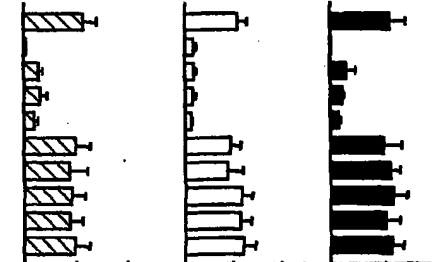
(Control-CpG) ODN
(Suppressive-CpG) ODN
(Control-CpG) ODN + CpG ODN
(Suppressive-CpG) ODN + CpG ODN

**d Suppressive ODN selectively block CpG DNA induced immune activation**

CpG ODN
CpG ODN + Suppressive ODN
Bacterial DNA
Bacterial DNA + Suppressive ODN
LPS
LPS + Suppressive ODN

**e Poly G's are critical for suppression**

CpG ODN 1.4
CpG ODN + TTAGGGTCAACCTTCA 3.4
CpG ODN + -AC- - - - -
CpG ODN + ACT- - - - -
CpG ODN + AAT- - - - -
CpG ODN + - - - - AA - - - -
CpG ODN + - - - - TT - - - -
CpG ODN + - - - - 1G - - - - 1.2
CpG ODN + - - - - 1G1G - - - - 1.0
CpG ODN + - - - - 1G1G1G - - - - 0.8

**f G-tetrad forming non-telomere sequences are also suppressive**

CpG ODN 1.4
CpG ODN + GGGTGGGTGGGTATTACCATTA 4.9
CpG ODN + TGGGCGGTTCAACCTTCA 4.1
CpG ODN + CCTCAAGCTTGAGGGG 4.6
CpG ODN + CCGGCCGGCCGGCCGG 2.8
CpG ODN + TTGGTTGGTTGGTTGG 3.2

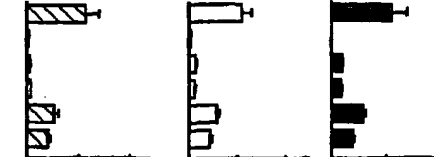


FIG. 10

IL-6 (ng/ml) IL-12 (ng/ml) IFN γ (pg/ml)

12/22

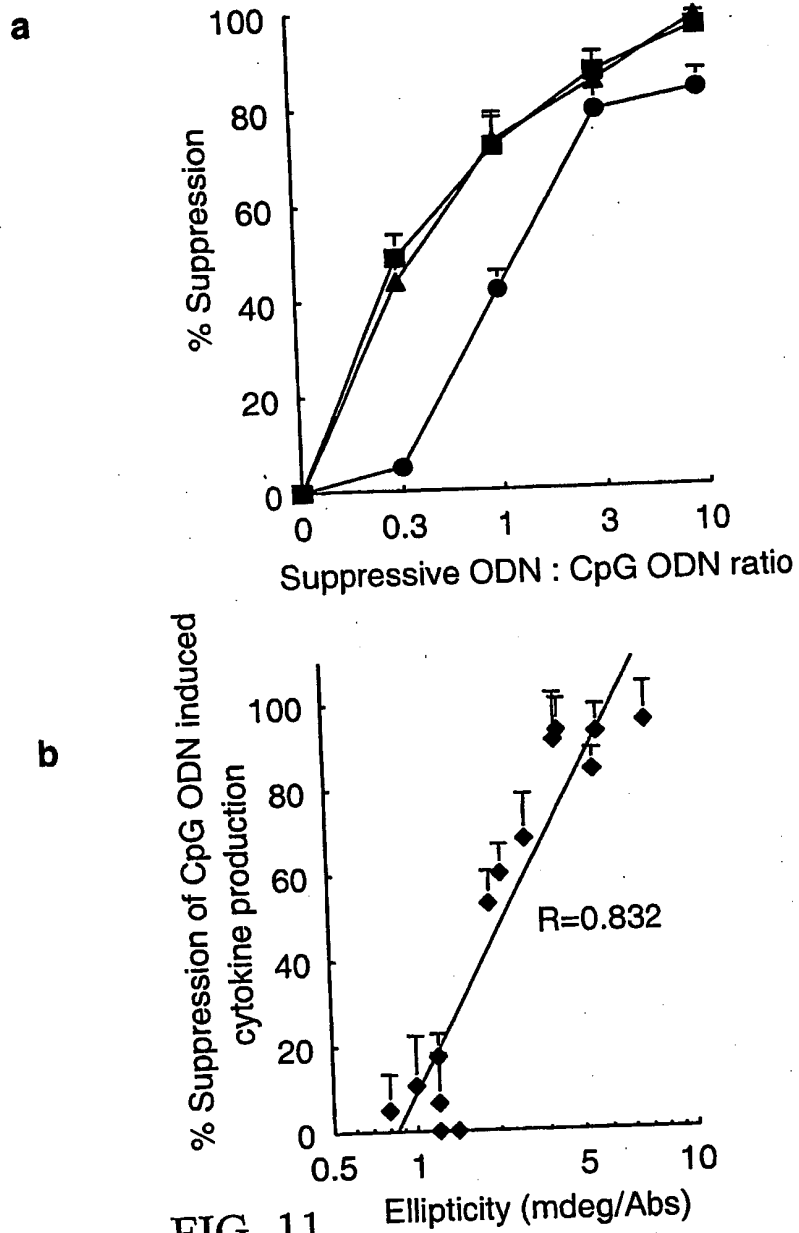
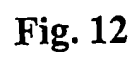


FIG. 11



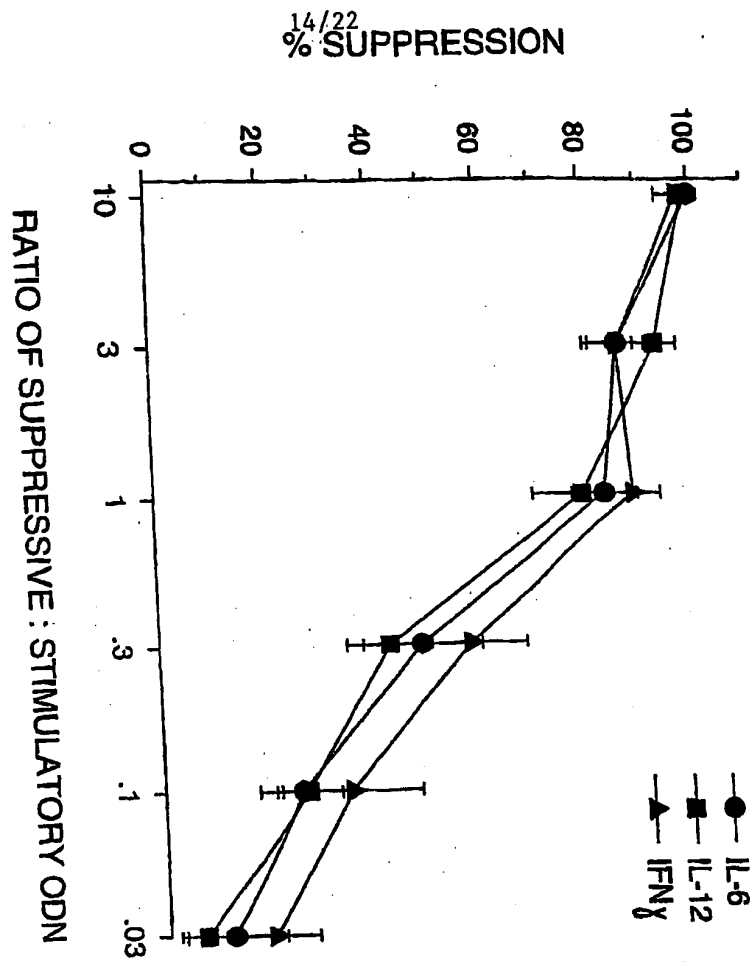


Fig. 13

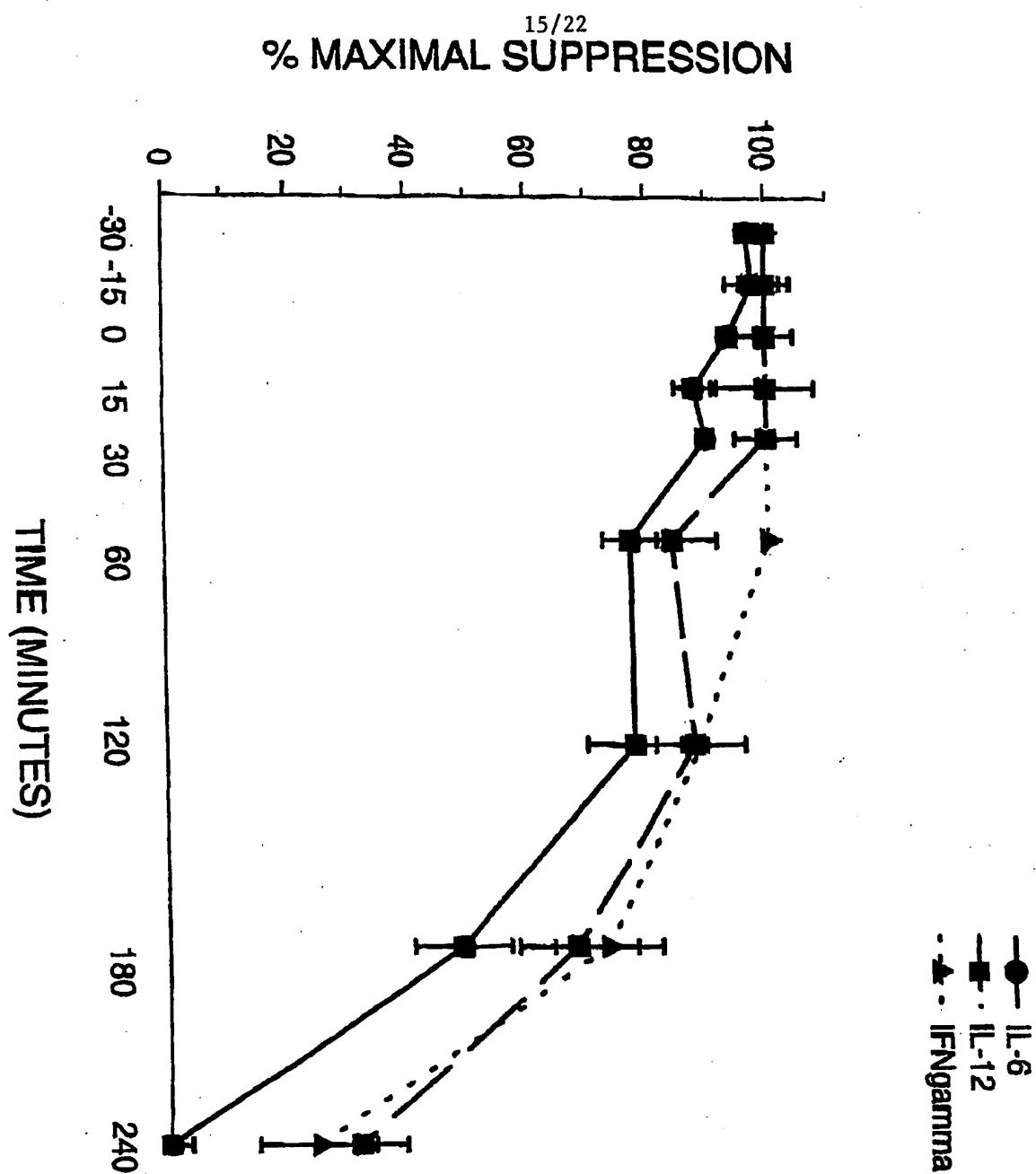


Fig. 14

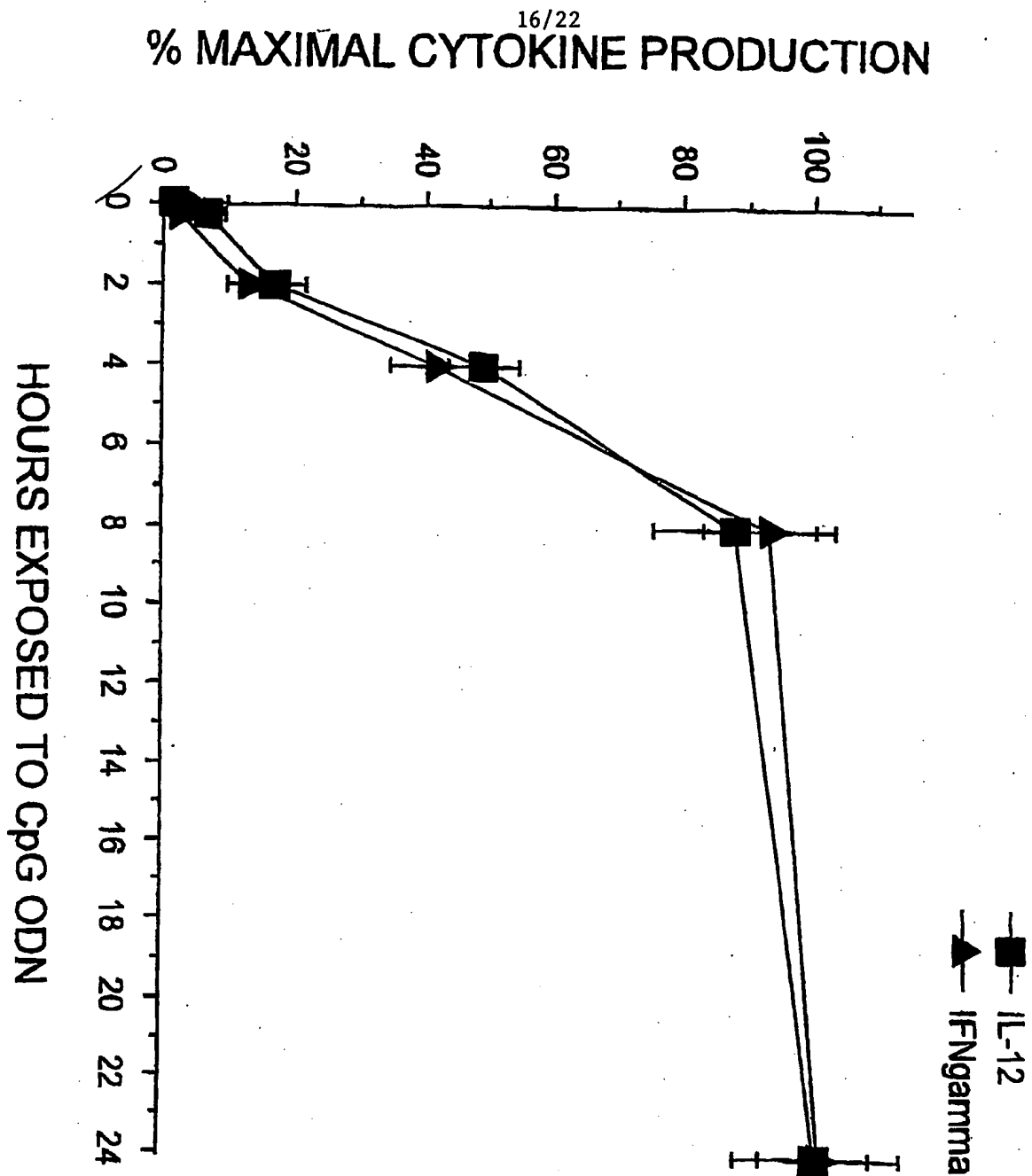


Fig. 15

17/22

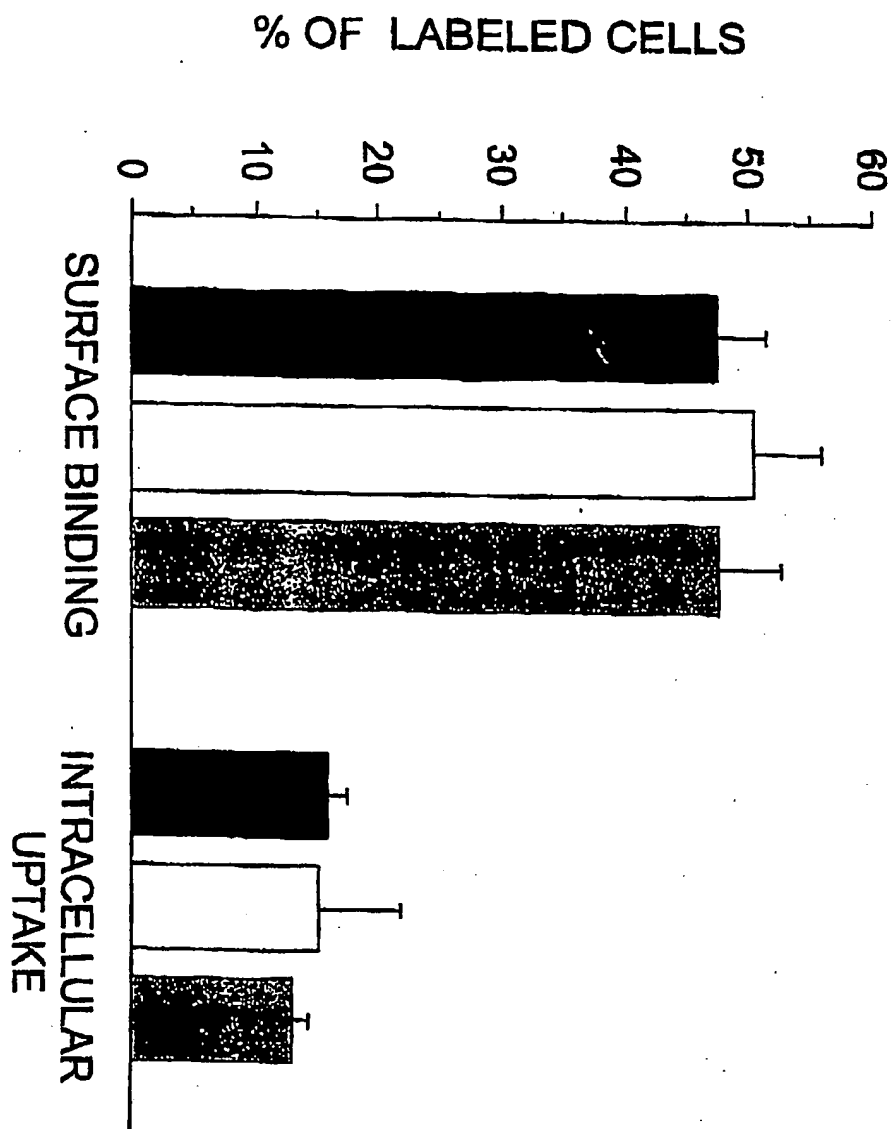


Fig. 16

18/22

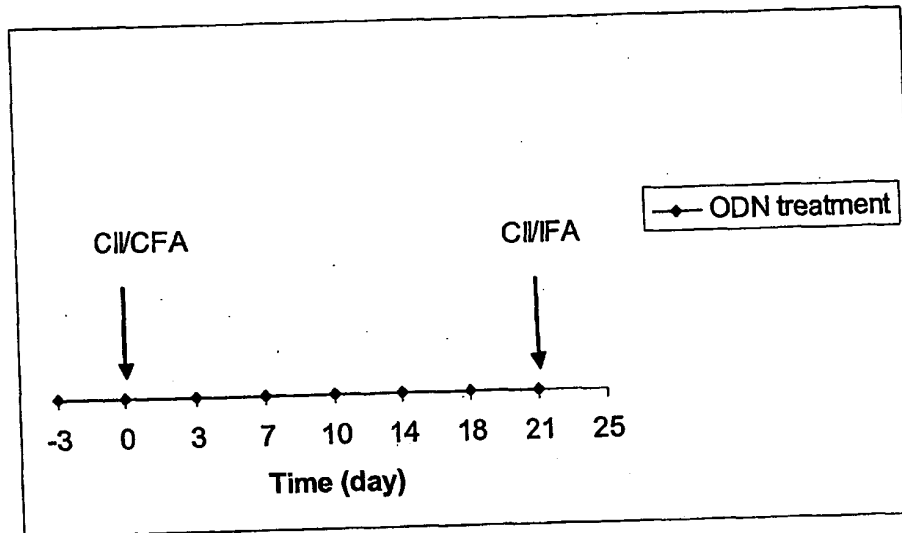


FIG. 17

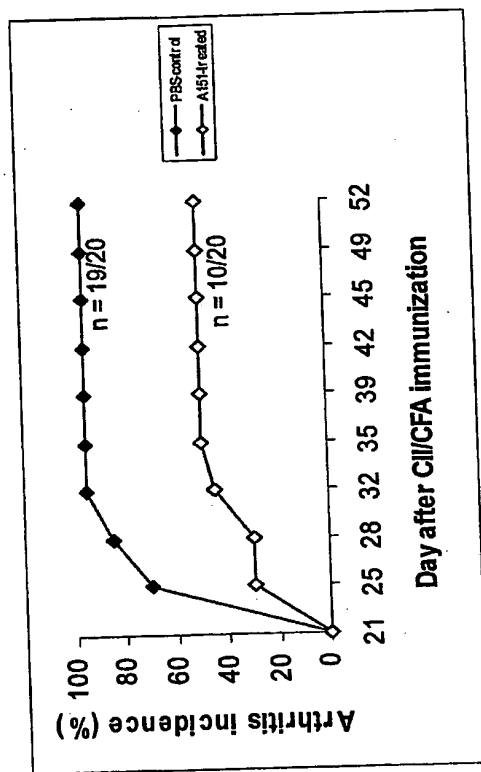


FIG. 18A

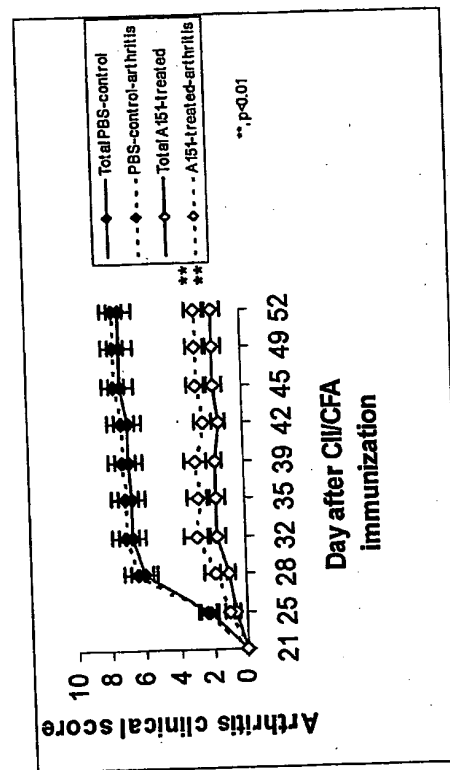


FIG. 18B

20/22

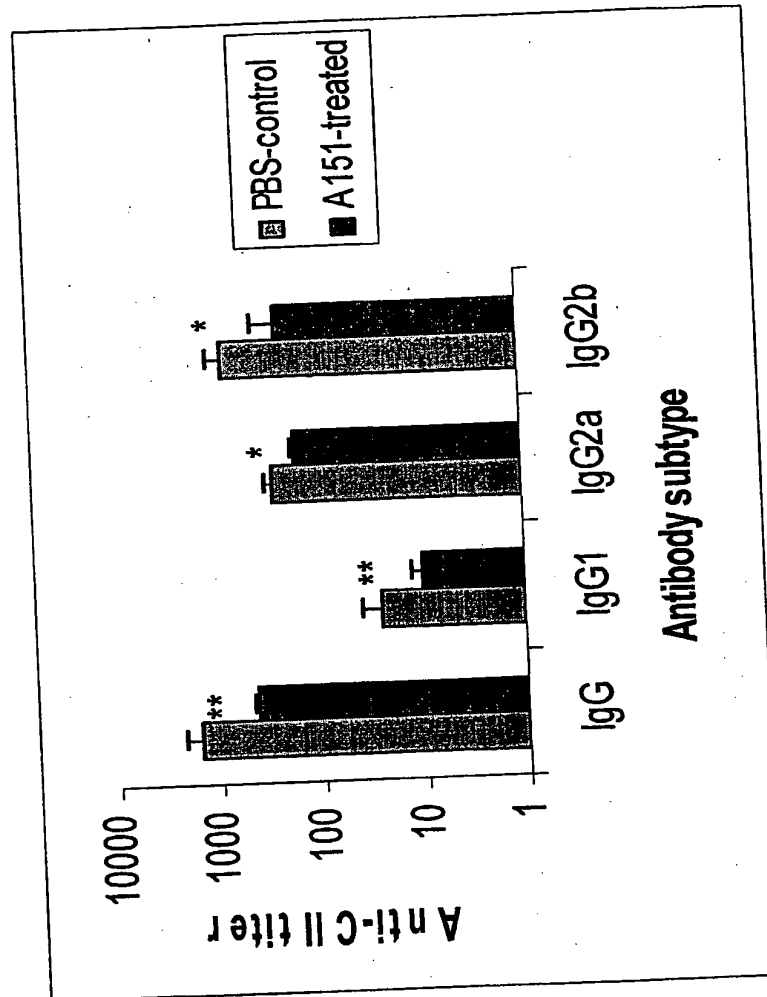


FIG. 19

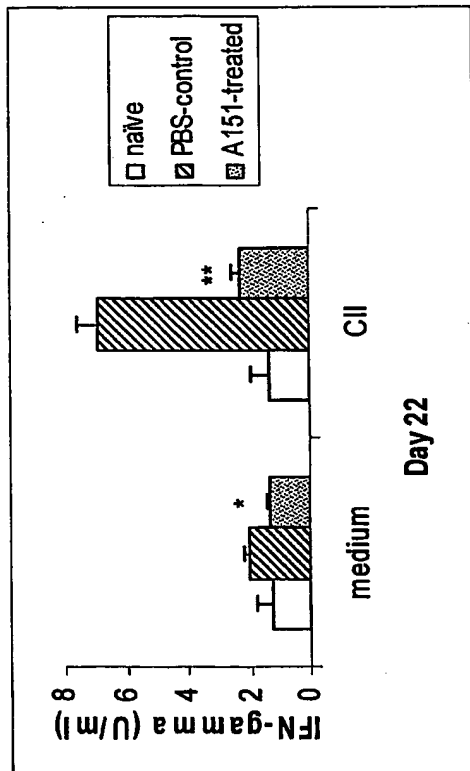


FIG. 20A

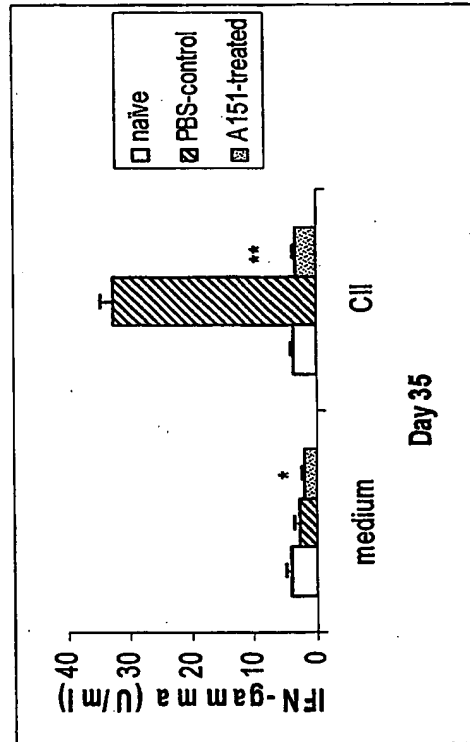


FIG. 20B

22/22

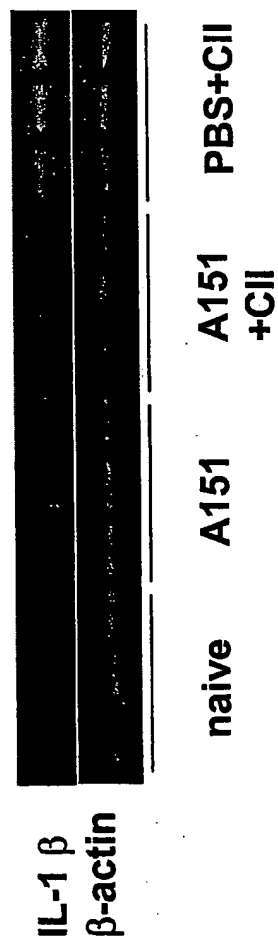


FIG. 21